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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/929,513	08/13/2001	Vivian F. Liu	23US	8239

7590 08/10/2005

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EXAMINER	
YANG, NELSON C	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/929,513	LIU ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 19, 2005 has been entered.

Response to Amendment

2. Claims 11-20 are pending.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

4. Claims 11-18, 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Chapman et al [US 6,627,461].

With respect to claim 11, Chapman et al teach a method for detecting a cellular event comprising coupling an electromagnetic test signal in a frequency range from 1 MHz to 1000 GHz to a sample, whereby said sample interacts with and modulates said test signal to produce a modulated test signal; detecting the modulated test signal; and analyzing said modulated test signal to detect a molecular or cellular event, wherein said coupling and detecting take place in a

temperature-controlled environment (claim 1), wherein the detection of the molecular or cellular event occurs in a region where both the radiating portion of the signal-generating circuit (signal line) and the receiving portion of the signal-detection circuit (ground elements) are coupled to the sample, thereby defining a detection region (claim 1), and wherein the signal path for the propagation of the electromagnetic signal may occur through coplanar waveguides (column 12, lines 23-31) at a single signal port that receives an incident test signal (column 12, lines 35-38). The sample can be cells (column 11, lines 35-45) located in reservoirs (column 23, lines 30-50).

5. With respect to claims 12, 13, the cellular activity may comprise include opening and closing of ion channels, leakage of cell contents, passage of material across a membrane (whether by passive or active transport), activation and inactivation of cellular processes, as well as all other functions of living cells (column 6, lines 8-15) and the detection of antibodies and carbohydrates (column 9, lines 5-10).

6. With respect to claims 14, 15, the cells may involve comparisons between a normal versus genetically modified cells.

7. With respect to claim 16, the modulated signals are obtained from two cells (or collection of cells) that differ in some fashion, for example by an added cell stimulant (column 6, lines 10-12).

8. With respect to claim 17, the detection may involve opening and closing of ion channels (column 6, lines 3-6).

9. With respect to claim 18, the cells may be from mammals (column 1, lines 40-50).

10. With respect to claim 20, Chapman et al teach verification with signals obtained from a collection of known proteins (column 25, lines 45-55).

11. Claims 11-14, 16, and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Hefti [US 6,566,079].

With respect to claim 11, Hefti teaches a method comprising a sample containing structure (fig. 1A) containing a sample comprising a ligand which may be contained within a molecular binding region which is electromagnetically coupled to a portion of a signal path, where the ligand may comprise cells, cellular constituents, cell membranes, cell adhesion molecules, organelles and synthetic analogues thereof (column 6, lines 20-24, 35-40). A protein is contacted with the ligand, and a response signal is detected, indicating a binding complex formed between the protein and the ligand, where the response signal results from coupling of the propagated signal to said protein, said ligand or said complex (claim 1, column 17, line 16). Coplanar waveguides may be used for propagation of the electromagnetic transmission signal, where transmission lines are formed from a material which can support the propagation of a signal over the desired frequency of operation (column 12, lines 20-40). The signal path may structurally comprise a signal plane consisting of a conductive layer or region, such as transmission lines, a ground plane, or a combination of both structures (column 9, lines 28-56). In particular, Hefti teaches a molecular binding region comprising cells that are coupled to the signal path (column 17, lines 40-50), where the coupling may involve a direct or indirect physical connection (cell plating) (column 10, lines 1-6). Specifically, Hefti teaches a specific embodiment where a detectable binding complex is only formed if a test ligand is able to bind to a receptor in a cell and trigger the expression of a reporter molecule which then binds to form the detectable binding complex (column 51, lines 1-5).

12. With respect to claims 12-14, 16, Hefti teaches a specific embodiment where a detectable binding complex is only formed if a test ligand is able to bind to a receptor in a cell and trigger the expression of a reporter molecule which then binds to form the detectable binding complex (column 51, lines 1-5). Specifically, Hefti teaches the construction of recombinant plasmid encoding a fusion protein created through the use of random oligonucleotides inserted into a cloning site of the plasmid. This cloning site is placed within the coding region of a gene encoding a DNA binding protein, such as the lac repressor, so that the specific binding function of the DNA binding protein is not destroyed upon the expression of the gene. The plasmid also contains a nucleotide sequence recognized as a binding site by the DNA binding protein. Thus, upon transformation of a suitable bacterial cell and expression of the fusion protein, the protein binds the plasmid which produced it. The bacterial cells are then lysed and the fusion proteins assayed for a given biological activity. Moreover, each fusion protein remains associated with the nucleic acid which encoded it; thus through nucleic acid amplification and sequencing of the nucleic acid portion of the protein/plasmid complexes which are selected for further characterization, the precise structure of the candidate compound can be determined (column 48, lines 19-42). Hefti further teaches cloning millions of variants of proteins or fragments thereof into a phage genome as a fusion to a gene encoding one of the phage coat proteins. Once expressed, the coat protein fusion products are incorporated into new phage particles that are assembled in the host bacterium. Subsequent incorporation of the fusion protein into the mature phage coat protein causes the ligand (e.g., peptide or peptide fragment) to be presented on the phage surface, while the corresponding genetic material resides within the phage particle. This

connection between displayed ligand and ligand genotype makes it possible to enrich for phage which display a ligand that binds a target of interest (column 48, line 58 – column 49, line 10).

13. With respect to claim 18, Hefti defines samples as including cells taken from any mammal (column 9, lines 1-10).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al [US 6,627,461] in view of Zang-Gandor [Zang-Gandor, Improved transfection of CHO cells, 1997, QIAGENnews, 4, 15-18].

Chapman et al teaches the use of samples comprising cells from mammals, as discussed above. Hefti does not teach the use of CHO wild-type cells.

Zang-Gandor, however, teach that CHO SSF cell lines are able to proliferate as suspension cultures in serum- and protein-free mediums, providing many advantages for economical, large-scale cultivation without expensive additives (p.15, pg.2 – p.l6, pg.1).

Therefore it would have been obvious to use CHO wild-type cells as suggested by Zang-Gandor in the method of Chapman et al, in order to achieve economical, large scale cultivation without incurring expensive additives.

16. Claims 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hefti [US 6,566,079] in view of Bodner et al [US 6,461,808].

Hefti teaches detecting cellular events, as discussed above. Hefti further teaches detecting changes such as binding events pH changes, temperature, ionic strength and the like (column 17, lines 50-56). Hefti fails to specifically teach detecting opening or closing of an ion channel.

Bodner et al, however, do teach detecting a change in amount of a substance (ions) present in the cell (opening and closing of ion channels) as a result of the presence of a test substance (antiligand) in a medium containing the cell (column 2, lines 49-67 and column 3, lines 13-41, claim 1). Bodner et al further teach that this methodology allows for the prediction of molecular and cellular events of biological and pharmaceutical importance that occur in physiological situations, such as in a cellular or subcellular membrane or in the cytosol of a cell (column 3, lines 43-50).

Therefore, it would have been obvious to detect the opening or closing of ion channels, as suggested by Bodner et al, in the method of Hefti et al, in order to allow for the prediction of molecular and cellular events of biological and pharmaceutical importance that occur in physiological situations, such as in a cellular or subcellular membrane or in the cytosol of a cell.

17. With respect to claim 20, Bodner et al further teach a step of verifying the method by correlating with a known cellular activity of a known substance (claim 2).

18. Claims 15 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hefti [US 6,566,079] in view of Zang-Gandor [Zang-Gandor, Improved transfection of CHO cells, 1997, QIAGENnews, 4, 15-18].

Hefti teaches the use of samples comprising cells from mammals, as discussed above. Hefti does not teach the use of CHO wild-type cells.

Zang-Gandor, however, teach that CHO SSF cell lines are able to proliferate as suspension cultures in serum- and protein-free mediums, providing many advantages for economical, large-scale cultivation without expensive additives (p.15, pg.2 – p.16, pg.1).

Therefore it would have been obvious to use CHO wild-type cells as suggested by Zang-Gandor in the method of Hefti, in order to achieve economical, large scale cultivation without incurring expensive additives.

Response to Arguments

19. Applicant's arguments filed May 19, 2005 have been fully considered but they are not persuasive. Applicant argues that although the binding of a reporter molecule to a ligand occurs within the cell cytoplasm, it still refers to a molecular interaction or molecular event (p.3). However, according to the specification, this would be considered a cellular molecular event (p.7, pg. 0006.6), which would indicate that the even is both a cellular event and a molecular event (p.7, pg. 0006.5). Furthermore, as claim 12 recites, the cellular activity being monitored is a change in amount of a cellular substance, namely the reporter molecule, as the result of presence of a test substance, a test ligand (column 50, lines 65 – column 51, line 5). Furthermore, Hefti provides an example of membrane changes, where incorporation of the fusion protein into the mature phage coat protein causes the ligand (e.g., peptide or peptide fragment) to be presented on the phage surface (column 48, line 58 – column 49, line 10), which would also be considered cellular activity (0006.4).

Conclusion

20. No claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
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08/07/05